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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,150	07/02/2007	Paul Kemp	DFBP:077US/11001670	5682

32425 7590 08/25/2010

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EXAMINER	
BERTOGLIO, VALARIE E	

ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
08/25/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/589,150	KEMP ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *13 May 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,13,15,17,20,55,58,59,62-64 and 71-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,13,15,17,20,55,58,59,62-64 and 71-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 August 2009* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's reply filed on 06/21/2010 is acknowledged. Claims 1-2,13,15,58-59,62-64 are amended. Claims 3-12,14,16,18-19,21-54,56-67,65-70 and 85-128 are cancelled.

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1,2,13,15,17,20,55,58-59,62-64,71-84 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The rejection is maintained for reasons of record set forth in the office action dated 12/21/09 and reiterated below.

The claims are drawn to a wound healing composition comprising cells having specific recited gene expression phenotypes. The specification teaches making a composition comprising fibroblasts, fibrinogen, aprotinin, thrombin and calcium chloride (Example 1). The specification teaches incubation of the composition over 16-24h prior to packaging (page 32). Packaging is discussed in Example 3, pages 34-36. At Example 4, the specification teaches gene expression analysis by differential display of fibroblasts in a collagen matrix, a fibrin matrix, and no matrix as well as the 'wound healing composition' (the fibrinogen, aprotinin, thrombin and calcium chloride composition of Example 1). Gene expression analysis was performed after various storage periods and the storage periods appear to have differentially affected gene expression. The claims recite that the matrix as a shelf life of at least 7 up to 28 days but does not limit the storage time to any particular period of time. A composition that is stored for up to 14 days would differ from that incubated more than 14 days. The gene expression profile claimed correlates

to Table 4. The results reported in Table 4, however, combine compositions that are made with collagen, fibrin or no matrix protein and pools data for compositions stored for less than, and greater than, 14 days. Because the samples are pooled samples, one of skill in the art would not know what exact conditions resulted in the claimed ranges. It is not clear how many of the cells were grown on collagen, how many on fibrin, etc. The specification fails to support that the claimed gene expression profile results from the claimed composition.

Furthermore, the specification has failed to demonstrate a "wound healing" phenotype, resulting from the claimed cells, that differs from fibroblasts in general. It cannot be determined, given the guidance in the specification, which conditions result in a wound healing phenotype. It appears the claims are drawn to a composition of cells that is changing in gene expression over time. It is not clearly enabled by the specification which cells and which gene expression levels will result in a desired wound healing phenotype.

Additionally, claim 62 is not fully supported by the specification as written. The claim requires incubation within a protein-rich environment for 7 to 14 days to allow development of a wound healing phenotype. This encompasses incubation at 37 degrees, for which the specification only teaches incubation for 16-24 hours before packaging and incubating at a lower temperature, i.e. 4 degrees. The specification fails to clearly establish when the 'wound healing' phenotype develops.

Applicant argues that claim 1 has been amended to more closely follow the teachings in the specification. In response, Applicant has amended the claims to recite that the cells are comprised within a matrix formed at 37C for about 16-24 hours. It is not clear how this amendment addresses the issues set forth above.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 62 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 62 remains unclear. It is not clear if the claim encompasses cells during the claimed storage period or if it is intended to encompass a composition after the storage period has expired.

All other previous rejections under this statute are rendered moot or withdrawn in light of Applicant's amendments or cancellation of claims.

Claims 1,2,12,15,17,20,55,58-59,62-64,71-84 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is unclear in use of the term "fibrinogen/isolated living dermal fibroblast mixture". It is not clear if the fibrin support matrix is formed with fibrinogen *or* dermal fibroblasts or both fibrinogen *and* dermal fibroblasts. It is not clear if the dermal fibroblasts of line 13 are the same as those of line 1. If the dermal fibroblasts are polymerized with the fibrinogen to make a support matrix, then the fibroblasts are part of the support matrix and it is not clear if additional dermal fibroblast cells of lines 1-2 are added to the support matrix already comprising dermal fibroblasts.

In claim 1, the phrase "at least 7 up to 28 days" is unclear. It is not clear if 28 is an absolute upper limit or if there is no upper limit. In other words, the phrase could be read as "at least 7 and up to 28" or "at least 7-28 or more".

Claims 2,12,15,17,20,55,58-59,62-64,71-84 depend from claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,2,13,15,17,20,55,58-59,63-64,71-73,76-78,81-84 are rejected under 35 U.S.C. 102(b) as being anticipated by Meana et al, (1998; IDS).

The instant rejection is not in contradiction to the above lack of enablement rejection. The claims are drawn to a composition and the art is applied to the extent that it appears to read on the claimed composition, particularly claims lacking any required methodology in obtaining the specifically recited gene expression profile. The specification fails to clearly set forth which methodology results in which expression levels, hence the lack of enablement. However, the art, as set forth below, appears to teach the same methodology, which would inherently result in the claimed characteristics.

Meana teaches, in section 2.2 at page 622, isolating human foreskin fibroblasts and culturing them on fibrin-containing gel between the 4th and 12th passage. The fibrin gel was made using 3ml of fibrinogen and 500,000 human fibroblasts and aprotinin in addition to thrombin and calcium chloride, the same conditions discussed in the specification (see page 28, Table 1). The gel was covered in media and either used or incubated for 24 hours prior to grafting. No specific conditions are recited in the claims to give the claimed characteristics. The same type of cells and matrix are used in Meana and in the specification. Therefore, it is considered that, while not explicitly recited in Meana, the fibroblasts of Meana inherently display the claimed characteristics, including the "wound healing phenotype" recited in the preamble.

Applicant argues that claim 1 has been amended to overcome the rejection. The amended claims now limit the support matrix to a fibrin support matrix, which is taught by Meana. The newly added limitation recites how this matrix was formed, however, there is nothing of record to show that a fibrin

support matrix made as claimed differs from that of Meana. Recitation of the shelf-life fails to limit the product as it is an inherent property of that which is claimed and would also be a property of that taught in the art. Applicant argues that the reference fails to disclose each and every recited limitation. However, Applicant fails to point out which limitations are not taught. Applicant argues that the limitations of claim 16 (not previously rejected) are included in claim 1. However, the newly added limitations are not the same as those of previously pending claim 16.

Claims 1,2,13,15,17,20,55,58-59,63-64,71-73,76-78,81-84 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 02/072113 (IDS).

The instant rejection is not in contradiction to the above lack of enablement rejection. The claims are drawn to a composition and the art is applied to the extent that it appears to read on the claimed composition, particularly claims lacking any required methodology in obtaining the specifically recited gene expression profile. The specification fails to clearly set forth which methodology results in which expression levels, hence the lack of enablement. However, the art, as set forth below, appears to teach the same methodology, which would inherently result in the claimed characteristics.

'113 teaches human fibroblasts and culturing them on fibrin (7.5 mg.ml)/thrombin-containing matrix for 24 hours. No specific conditions are recited in the claims to give the claimed characteristics. The same type of cells and matrix are used in '113 and in the specification. Therefore, it is considered that, while not explicitly recited in '113, the fibroblast cell composition of '113 inherently display the claimed characteristics, including the "wound healing phenotype" recited in the preamble.

Applicant argues that claim 1 has been amended to overcome the rejection. The amended claims now limit the support matrix to a fibrin support matrix, which is taught by '113. The newly added limitation recites how this matrix was formed, however, there is nothing of record to show that a fibrin support matrix made as claimed differs from that of '113. Recitation of the shelf-life fails to limit the

product as it is an inherent property of that which is claimed and would also be a property of that taught in the art. Applicant argues that the reference fails to disclose each and every recited limitation. However, Applicant fails to point out which limitations are not taught. Applicant argues that the limitations of claim 16 (not previously rejected) are included in claim 1. However, the newly added limitations are not the same as those of previously pending claim 16.

Claims 1-2,13,15,17,20,55,58-59,63-64,71-73,76-78,81-84 are rejected under 35 U.S.C. 102(b) as being anticipated by Tuan et al (1996; IDS).

The instant rejection is not in contradiction to the above lack of enablement rejection. The claims are drawn to a composition and the art is applied to the extent that it appears to read on the claimed composition, particularly claims lacking any required methodology in obtaining the specifically recited gene expression profile. The specification fails to clearly set forth which methodology results in which expression levels, hence the lack of enablement. However, the art, as set forth below, appears to teach the same methodology, which would inherently result in the claimed characteristics.

Tuan teaches human foreskin fibroblasts and culturing them on fibrin/thrombin-containing matrix. No specific conditions are recited in the claims to give the claimed characteristics. Human skin fibroblasts were added to a fibrinogen solution. Final concentrations of fibrinogen and fibroblasts were 2.5 mg/ml and 1 x 10^6 cells/ml, respectively. Aliquots (0.1 ml) of the fibroblast/fibrinogen mixtures were placed in wells of 48-well tissue culture plates (Costar, Cambridge, MA) with 1 unit of thrombin per sample. The preparations were subsequently incubated at 37 degrees. The same type of cells and matrix are used in Tuan and in the specification. Therefore, it is considered that, while not explicitly recited in '113, the fibroblast cell composition of '113 inherently display the claimed characteristics, including the "wound healing phenotype" recited in the preamble.

Applicant argues that claim 1 has been amended to overcome the rejection. The amended claims now limit the support matrix to a fibrin support matrix, which is taught by '113. The newly added limitation recites how this matrix was formed, however, there is nothing of record to show that a fibrin support matrix made as claimed differs from that of '113. Recitation of the shelf-life fails to limit the product as it is an inherent property of that which is claimed and would also be a property of that taught in the art. Applicant argues that the reference fails to disclose each and every recited limitation. However, Applicant fails to point out which limitations are not taught. Applicant argues that the limitations of claim 16 (not previously rejected) are included in claim 1. However, the newly added limitations are not the same as those of previously pending claim 16.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 79-80 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Meana (1998, IDS) in view of Muhart (1999, IDS).

The teachings of Meana are set forth above. Meana did not teach a flexible pouch container. However, Muhart taught packaging a similar wound healing composition in a flexible pouch container for shipping.

One of skill in the art would have found it obvious to combine the teachings of Meana with those of Muhart to arrive at the claimed composition of a matrix of fibroblast cells packaged in a flexible container. One would have been motivated to make such a combination as the container provides a means for storage and transport of the claimed composition.

Applicant refers to the arguments set forth for the rejection of parent claims under Meana (above). This rejection is maintained for reasons set forth above.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Valarie Bertoglio/
Primary Examiner, Art Unit 1632